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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 10/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/886,899	LOVELL-BADGE ET AL.	
	Examin r	Art Unit	
	Jeffrey Fredman	1634	

-- Th MAILING DATE of this communication appears on the cover she t with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *9-15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. Applicant's submitted priority document is acknowledged.

Double Patenting

2. Claims 1-8, 16 and 17 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of copending Application No. 09/464,146. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-8 of copending Application No. 09/464,146 teach a broad method of isolating cells by detecting expression of Sox-1 in the cells and sorting the cells to isolate those expressing Sox-1. This narrower species claim anticipates, and consequently renders obvious, the broader generic claim currently pending, in which any Sox gene can be identified and sorted. The only difference between the claims is that the current claim 1 requires the cell to be pluripotent while the claims of copending Application No. 09/464,146 are neuroblastic cells. But the specification of copending Application No. 09/464,146 makes clear at page 3, line 8, for example, that neuroblast cells are pluripotent and therefore fall within the scope of the pending claims. Therefore, the neuroblastic cells are themselves a species in the genus of pluripotent cells and anticipate, and consequently render obvious that genus.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-8, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or

absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a method of isolating a subset of pluripotent cells which express Sox genes. The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

The claims broadly encompass the use of any pluripotent cell derived from any organism whatsoever and any Sox gene. Further, the claims are broadly drawn to the use of sorted cells.

Any pluripotent cell

The method broadly encompasses the use of the method in any type of pluripotent cell whether that cell is of hematopoietic origin, neural origin, of ectoderm or endoderm. This breadth is striking and extreme, since the invention presumes that cells intending to develop into any particular tissue type will commit to that lineage using the same set of genetic elements. For example, that a myoblast, which is a pluripotent cell, which can differentiate into a myocyte upon addition of MyoD, will differentiate according to the same program as a neuroblast, a kidney precursor cell, or hematopoietic stem cells. Further, the cells may be from either embryos, from developing organisms or may represent pools of pluripotent cells in adult organisms. In adults, the cells undergoing the test may be subject to any of a variety of different conditions depending upon the particular patient studied, with insulin dependent patients, for example receiving daily doses of a compound which significantly alters

cellular metabolism while cancer patients may be receiving chemotherapeutic treatments, pain medicine for surgery, corticosteroids to reduce trauma associated with surgery which themselves significantly impact cellular metabolism or any of a number of other complicating factors which impact the expression of cellular markers such as the Sox genes.

Any organism

The method not only encompasses the use of any pluripotent cell, but is open to cells from any organisms. While the prior art (see Wegner et al (Nucleic Acids Research (1999) 27(6):1409-1420) shows that Sox genes are present in a variety of different organisms and that some are involved in differentiation, the breadth of the claim encompasses not only animals but insects, plants and developmental microorganisms. The claim is sufficiently broad to encompass any living thing which develops, whether that is a slime mold, a mouse or a cedar tree.

Wide variety of Sox genes

The claimed method also broadly encompasses any Sox gene from table 1 as well as Sox 15 and 16. However, the claims are not limited to the human sequence, but broadly encompass the equivalent Sox genes from multiple species, since the claims do not include accession numbers or sequences. While Wegner indicates that 20 such genes have been identified in mouse and man, if every mammal has it's own set of 20 such genes, in a world that has about 4,000 mammalian species, there are 80,000 different mammalian Sox genes. This figure does not include any from the tens of thousands of insect species, of plant species, of reptiles and fish, of birds, and of other organisms.

Sorted cells

The claims are also drawn to a broad use of sorted cells, after detection by some means. Since only two modes are known for detection followed by FACS sorting in the prior art, which rely on either antibody or nucleic acids for the detection, and no additional disclosure is provided in the specification on methods of such sorting, the claims are limited to the prior art methods, which all teach the use of dead cells. As Bauer et al (Analysis of Intracellular Proteins, Chapter 23, in "Methods in Cell Biology", Volume 41 – Flow Cytometry, Second edition, Part A, 1995, pages 351-376) teaches, detection of the Sox protein using antibodies requires permeabilization and fixation of the cells in order for the antibody to enter the cell to interact with the intracellular antigen, followed by washing steps in order to ensure that only cells which have the antigen are specifically stained (see page 364).

Quantity of Experimenation

The quantity of experimentation in this area is large since there is significant variability in the function and activity of each of the Sox genes in each of the cell types and different cellular sources. For example, Pevny (Development (1998) 125:1967-1978) teaches that Sox1 is, in P19 cells, associated with differentiation and directs the P19 cells to their neural fate (see page 1972, column 2). In contrast, Nishiguchi et al (Genes and Development (1998) 12:776-781) teaches that Sox1 is a direct regulator of lens development in mice (see page 77, column 2). Lastly, Wood et al (European J. Neuroscience (2000) 12(11)p258) teaches that Sox1 is required for migration of certain neural cells which results in an epileptic phenotype (see abstract). Thus, the prior art shows that even for a single Sox gene, there are multiple different cells which the gene

effects to result in multiple different phenotypes. In order to use any given Sox gene, abundant and inventive experimentation would be necessary in order to determine the biological and molecular roles of the molecule. This experimentation would require years of inventive effort to develop any use for the sorted cells beyond a template for further research.

The unpredictability of the art and the state of the prior art

The art teaches that it is entirely unpredictable what function Sox genes have in cells. As noted above, Pevny, Nishiguchi and Wood each had different functions for the same Sox gene, Sox1. Wegner, also cited previously, amplifies this unpredictability by showing the broad range of cell types and effects with which Sox genes are implicated (see page 1413, table 2). For example Sox 4 is involved in hear differentiation, thymus, and immune cells, while Sox 10 is involved in melanoblasts, schwann cells and neural cells (see page 1413, table 2). Given the unpredictability found in the known Sox genes, it is even more unpredictable what effects as yet unidentified Sox genes in the tens of thousands of different possible cells would have. For example, it is entirely unpredictable what effects any particular Sox gene or protein will have on the cell which contains the Sox gene or protein. Wegner supports this unpredictability, noting "Thus, it is generally difficult to make statements about the nature of a particular Sox protein other than a preliminary classification, as long as it is only known from its HMG domain (see page 1412, column 1, last sentence to page 1412, column 2). This express statement of the unpredictability in functional analysis of the Sox genes is enhanced by Wegner's comment that "Functional redundancy is a recurring theme with Sox proteins (see page 1413, column 1)". When the full scope of the claim is realized, focusing on the millions of different Sox genes found in millions of different multicellular organisms

and relying upon millions of different possible developmental precursor cells, the full breadth of the claim supports the unpredictability argument. If the role of Sox1 in a single organism is so multivariate and unpredictable and if Wegner expressly indicates that the nature of a Sox protein is difficult to predict from its structure, then it is even more unpredictable to identify the role of such proteins in the millions of other species which are included in the scope of the claim.

A separate area of unpredictability concerns the isolation and sorting of the Sox expressing cells. As noted above, the prior art such as Bauer only enables the sorting of dead cells. This is significant because the claim requires isolation of "a pluripotent cell". The dead cells identified by Bauer are not, and cannot be, "pluripotent" because that term requires the cell to be capable of further growth and differentiation. This definition is supported by the specification, which notes on page 3 that "As used herein, a "pluripotent cell" is a cell which may be induced to differentiate, in vivo or in vitro, into at least two different cell types." Thus, it is unpredictable how a "pluripotent" cell can be isolated using a intracellular marker without killing the cell and thereby rendering the cell not "pluripotent". This hidden conflict and unpredictability in the claim is apparent when the prior art such as Bauer is analyzed to demonstrate that all isolation methods for intracellular proteins and hybridization techniques require the permeabilization and fixation of cells, which kill the cells. Since dead cells cannot be pluripotent, it is unpredictable how such cells are isolated.

Working Examples

The specification has no working examples of isolation of pluripotent cells by detection of Sox gene expression followed by sorting of the cells.

Guidance in the Specification.

The specification teaches a particular list of known Sox proteins and genes. The specification discloses that there is some level of structural relationship between Sox genes based upon the HMG motif. The specification, however, does not teach the sequence of Sox genes from even a representative fraction of all of the different organisms which are included in the scope of the claim, nor are a representative number of precursor cell types given. The specification itself focuses on Sox1 and neural differentiation. While the specification does have a table on pages 14-16 which discusses 24 Sox genes and lists a few different species in which these genes are found, in only a very few of these situations is any biological role known.

Separately, the specification, while mentioning the use of flow cytometry or FACS for cell sorting, provides no disclosure of how to isolate living pluripotent cells instead of dead, fixed and permeabilized cells. No particular techniques for sorting or tagging are given in the specification and the specification lacks any additional teaching not found in the prior art for such isolation and sorting methods.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the use of and sorting of Sox genes combined with the large quantity of experimentation support a conclusion of undue experimentation. Further, the specification provides one with no written description or guidance that leads one to a reliable method of sorting Sox

expressing cells to result in "pluripotent" cells as required by the claim and defined by the specification. One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Further the specification does not provide guidance to overcome art recognized problems in the use Sox genes as predictable markers as discussed by Wegner. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working examples and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-8 and 16, 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in

possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The genus includes variants for which no written description is provided in the specification since the genus is open to any allelic variant of the current Sox genes as well as any new Sox gene discovered in any species whatsoever. Thus, applicant has express possession of only twenty or so particular Sox genes in a genus which comprises hundreds of millions of different possibilities. Here, there is one common structural element, the presence of an HMG domain, but there are no functional limitations whatsoever on the proteins.

Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of Sox genes in the specification is entirely functional. The specification states on page 12 that "As used herein, a "Sox coding sequence" refers to a nucleic acid sequence that in its native state or in a recombinant form can be transcribed and/or translated to produce a SOX mRNA and/or the SOX polypeptide or a fragment thereof." Thus, the definition in the specification of a Sox sequence is entirely functional without any structural requirements. The art does require an HMG box. Therefore, the specification is claiming a material which is known to exist but specific knowledge of what a "SOX" protein or nucleic acid consists of is absent.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

The current situation is a definition of the compound solely but its functional utility, as a "Sox" gene or protein, without any definition of the particular structure required.

In the instant application, certain specific SEQ ID NOs are described. Also, in Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which comprise Sox genes or proteins. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Response to Arguments

7. Applicant's arguments filed August 25, 2003 have been fully considered but they are not persuasive.

Applicant argues that Sox gene expression has been found in a wide variety of tissues and that Genbank accession numbers for 22 Sox genes are provided in the specification. With regard to the variety of cells, the scope still remains complete, with the claims encompassing any cell. It is clear that expression of some Sox genes in a variety of tissues was known in the prior art.

With regard to the breadth and unpredictability of the claimed Sox genes, the claims are not limited to the specific Accession numbers claimed. In fact, the claims

are not limited to the human Sox genes. Applicant cites Wegner to show that Sox genes are involved in a variety of developmental processes. However, Wegner also shows the ambiguous and unpredictable nature of a term such as Sox9. For example, Wegner states "Sox9 has been used to describe a group E PCR fragment from mouse (accession no. Z18958) and a group B fragment from man (accession no. X65665). (see page 1412, column 2). Wegner relates similar confusion for Sox8, Sox10, Sox19 and Sox21, as well as even more confusion for Sox12. Therefore, when the amended claim is drawn to Sox9 for example, which Sox9 is meant. Is it the mouse Group E fragment with accession no. Z18957 meant or is it the human Group B fr. Those are the two accession numbers for Sox9 provided by Wegner. In Applicant's response, Applicant provides yet a third accession no. S74504/5/6 for Sox9 which is a human sequence. This sequence, according to a Blast alignment, lacks any significant sequence similarity with the Group B fragment from man above of accession no. X65665, but has some similarity to Z18958 of mouse.

So when Applicant claims Sox9, for example, the breadth of that claim reads not only on accession no. S74504 disclosed in the specification, nor even only to the mouse Group E and human Group B Sox9 genes discussed above, but also includes any gene in any organism which is the 9th Sox gene discovered for that organism, based on the notation of Wegner. (see page 1410, "Numbers are assigned to Sox proteins consecutively in the order of their identification, with the count being now at 24."). So this claim will read on a method using the Sox9 of swordtail fish, of elephants and of

koala bears, even though those sequences are entirely unpredictable, unknown, and may share no significant homology with human Sox9.

Applicant's then argue that the specification teaches a particular method of recovery of viable cells using G418 selection. Because claim 8 continues to recite FACS analysis, the claims expressly encompass methods which would not be expected to function for the reasons given in the rejection. Therefore, with regard to this element of the enablement rejection, it is really a scope of enablement. Applicant is correct and is enabled for the specific G418 selection method disclosed. However, the claim is not limited to that selection method as expressly demonstrated by dependent claim 8. Therefore, Applicant is arguing a limitation not found in the claim which does not overcome the scope of enablement issue with regard to this element.

Applicant argues the quantity of experimentation factor by stating that the claims do not require knowledge of the biological and molecular roles of Sox genes. This is incorrect, since the claims expressly operate by sorting for pluripotent cells by Sox gene expression. While some Sox genes are associated with sorts of development, some are merely associated with disease (see Wegner, table 2), and the claimed method will not operate unless the specific Sox gene being analyzed is associated with development.

Applicant then argues the unpredictability factor based upon limiting the claims to the named Sox genes and based upon the single G418 selection method taught. For the reasons given above, the g418 selection method is a scope of enablement issue, and does not weaken the unpredictability of the method against the full scope of the

claim which expressly includes FACS analysis as shown by claim 8. Also as discussed more fully above, simply naming a molecule, where the nomenclature is based upon order of discovery, will not result in a related group of Sox genes, but rather, will often result in genes of radically different function in different organisms having the same name.

With regard to the working examples, the sole G418 method is the same scope of enablement issue argued above.

Applicant concludes by arguing the written description rejection. However, for many of the reasons given above, the claims still encompass undescribed embodiments. For example, a claim to Sox9 or Sox15 clear encompasses the 9th or 15th discovered Sox gene based upon the nomenclature of Wegner. Given this fact, there is no predictability of sequence, function or structure based upon the name. Further, in Lilly, two genes with known correlated function, the human and mouse insulin genes, where the sequence of one was known but not the other, led to a conclusion that a claim encompassing both lacked written description, even though the genes were 80% identical. Here, where the Sox9 gene of human need not have any correlated function with the Sox9 gene of mouse, cow, pig, sheep, zebra or elephant (all of which fall within the claim). There is no evidence suggesting any structural relationship and, in fact, the teaching of Wegner that "Numbers are assigned to Sox proteins consecutively in the order of their identification (see page 1410, column 1)" teaches that there is no structural or functional relationship between Sox proteins of the same number between different species. Finally, even within humans, there are allelic

variants, alternate splices and other variations, none of which are disclosed in the specification. For these reasons, the written description rejection is maintained.

Conclusion

8. Applicant's amendment necessitated the new arguments or ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jeffrey Fredman
Primary Examiner
Art Unit 1634